IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TEXAS
WACO DIVISION

RAVGEN, INC., *Plaintiff*	§	
-vs-	§	1:20-CV-00692-ADA
NATERA, INC. AND NSTX, INC.,	§	
Defendants.	§	

MEMORANDUM OPINION AND ORDER

Defendant Natera moves for summary judgment of invalidity of Claims 125 and 132 of the '277 Patent based on patent eligibility under 35 U.S.C. § 101. Dkt. 340. The Court heard the parties' arguments during the final pretrial conference held on December 11, 2023, and orally denied Natera's motion. Consistent with the Court's earlier oral ruling and omnibus order at Dkt. 458, the Court **DENIES** Natera's Motion under Mayo Step 1 for the reasons set forth below.

Natera argues the claims are directed to natural phenomena and do not introduce any meaningful non-routine steps. Dkt. 340 at 1–2. For Claim 125, Natera identifies the natural phenomenon as "'detecting the presence or absence of a fetal chromosomal abnormality' using 'a sample from a pregnant female.'" *Id.* at 1 (quoting Claim 1). For Claim 132, Natera identifies "determining the sequence of a locus of interest on free fetal DNA isolated from a sample from a pregnant female." *Id.* For the reasons discussed below, the Court disagrees that the claims are directed to a natural phenomenon and finds there are genuine issues of material fact as to whether the claims introduce meaningful non-routine steps.

I. LEGAL STANDARD

The Supreme Court in *Mayo Collaborative Servs. v. Prometheus Labs, Inc.*, 566 U.S. 70 (2012) set forth a framework for determining patent eligibility. The determination is based on two steps: 1) whether the patent is directed to a patent-ineligible concepts, and if so, 2) whether there are additional claimed elements that transfer the nature of the claim into a patent-eligible application. *Id.* at 71-72. Step 2 requires more than "well-understood, routine, conventional activity." *Id*. at 73.

II. ANALYSIS

Claim 125 depends from Claims 1 and 8 *inter alia*, which recite:

> 1. A method for detecting the presence or absence of a fetal chromosomal abnormality, said method comprising: quantitating a ratio of the relative amount of alleles at a heterozygous locus of interest in a mixture of template DNA, wherein said mixture comprises maternal DNA and fetal DNA, and wherein said mixture of maternal DNA and fetal DNA has been obtained from a sample from a pregnant female, and further wherein said heterozygous locus of interest has been identified by determining the sequence of alleles at the locus of interest, and wherein said ratio indicates the presence or absence of a fetal chromosomal abnormality.
>
> 8. The method of claim 4, wherein said sample is mixed with an agent that inhibits cell lysis to inhibit the lysis of cells, if cells are present, wherein the agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor.

Claim 125 recites:

> 125. The method of claim 10, wherein said cell lysis inhibitor is selected from glutaraldehyde, formaldehyde and formalin.

Natera argues the focus of the claim is detecting a fetal chromosomal abnormality, which is recited in the preamble of Claim 1. Dkt. 361 at 4–5. Ravgen argues that the focus of the claim when analyzed as a whole is "preventing cell lysis during sample preparation to improve the process of preparing and analyzing cell-free DNA." Dkt. 384 at 7. Natera responds that the only claimed preparation step is the addition of an agent, and the addition of an agent is not the focus of the claim because the claims provide no requirements on how to use the claimed agent such as how

much should be added, how long it should be applied, and how the sample should be handled. Dkt. 427 at 2–3.

Both parties acknowledge that the Section 101 analysis must focus on whether the claims as a whole are directed to a natural phenomenon. *See Synopsis, Inc. v. Mentor Graphics Corp.*, 839 F.3d 1138, 1149 (Fed. Cir. 2016). And both parties cite cases with claims related to biological processes to support their arguments. Natera cites *Ariosa Diagnostics, Inc. v. Sequenom, Inc.* in which the Federal Circuit held claims directed to detecting paternally inherited nucleic acid patent ineligible because "the claims are directed to matter that is naturally occurring." 788 F.3d 1371, 1376 (Fed. Cir. 2015). Ravgen cites *Rapid Litigation Management Ltd. v. Cellzdirect, Inc.* in which the Federal Circuit held claims directed to freezing and thawing hepatocytes to be patent eligible. 827 F.3d 1042, 1048 (Fed. Cir. 2016). In *Rapid Litigation*, the Federal Circuit determined the claims were not simply directed to observing or detecting "the ability of hepatocytes to survive multiple freeze-thaw cycles," but rather that the claims as a whole were directed to "a new and useful method of preserving hepatocyte cells." *Id.*

In both *Ariosa Diagnostics* and *Rapid Litigation*, the claims at issue recite steps in addition to detecting natural phenomena. In *Ariosa Diagnostics*, the additional step is amplifying DNA. *Ariosa Diagnostics*, 788 F.3d at 1373–74. In *Rapid Litigation*, the additional step is preserving hepatocyte cells. *Rapid Litigation*, 827 F.3d at 1046. The parties dispute whether Claim 125 is more like the claims in *Ariosa Diagnostics,* which were held patent ineligible, or the claims in *Rapid Litigation*, which were held patent eligible. In this case, Claim 125, including the limitations of the claims from which it depends, recites steps for preserving the cell structure of blood during the process of detecting abnormalities. Because Claim 125 recites steps for preserving a sample, the Court concludes it is more like the claims of *Rapid Litigation* rather than *Ariosa Diagnostics*.

Natera takes an unduly narrow view of Claim 125 by focusing on the preamble of Claim 1 rather than Claim 125 as a whole. The preamble recites detecting chromosomal abnormalities in a sample, but the claim also recites preparation steps to inhibit cell lysis by mixing an agent with the sample. Like the claims in *Rapid Litigation*, which recite steps for preserving cells, Claim 125 recites steps for preserving the cell structure of blood during the process of detecting abnormalities. For example, Claim 8 from which Claim 125 depends, recites mixing a sample with an agent that inhibits cell lysis. As the specification provides, the ability to detect fetal abnormalities was hindered by the low percentage of fetal DNA in a sample, and the addition of cell lysis inhibitors preserved the cell structure of fetal DNA and thereby increased the percentage of fetal DNA. '277 Patent, Cols. 32:33–39, 89:1–11.

For the above reasons, the Court concludes Claim 125, when taken as whole, is directed to a method for preserving the cell structure of blood during the process of detecting abnormalities. Claim 125 is thus not directed to a natural phenomenon.

Even if Claim 125 were directed to a natural phenomenon, Natera fails to show that there are no genuine issues of material fact as to whether the limitations of the claim transform the claim into a patent-eligible application of the natural phenomenon. Again, this analysis must be based on the claim as a whole. In particular, the analysis must "consider the elements of each claim both individually and 'as an ordered combination' to determine whether additional elements 'transform the nature of the claim' into a patent-eligible application." *Ariosa Diagnostics*, 788 F.3d at 1375–76 (quoting *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 78–79 (2012))

Natera argues that the recited limitations including sequencing, adding an agent, quantitating allele ratio, and detecting abnormalities were routine and conventional. Dkt. 361 at 13. But aside from attorney argument, Natera does not cite any evidence that the combination of

the claimed elements was routine and conventional. *See* Dkt. 427 at 5 ("There is nothing in the 'ordered combination' of applying the indisputably known concept of using 'agents' like formaldehyde to prevent cell lysis that makes the claims patent eligible.") *see also* Dkt. 361 at 13 (arguing without citation that the claim "taken as a whole" is not inventive). Natera cites cases finding claims in different patents to recite routine and conventional steps; however, this analysis is fact intensive, and analogizing Claim 125 to other claims in other patents is not sufficient to show there is no genuine issue of material fact here.

On the other side, Ravgen's expert opines that using agents during sample preparation for cell-free DNA applications was not a well-known routine or conventional step. *See* Dkt. 384-7 at ¶ 1919. The Court also notes that Natera filed an *inter-partes* review (IPR) in which the PTAB found that a person of ordinary skill would not have been motivated to combine the use of a cell lysis inhibiting agent with cell-free DNA analysis methods. *See* Dkt. 384-4 at 63. The Court recognizes that the issues in dispute in the IPR are different and are not co-extensive with this analysis, but the Court finds that the similarity between a claim being non-obvious and whether the claim when taken as a whole is routine and conventional supports a finding that there are genuine issues of material fact. In any event, on Natera's motion for summary judgement, the Court views the unrebutted evidence from Ravgen's expert in the light most favorable to Ravgen, which further supports the Court's finding.

For the above reasons, the Court holds Claim 125 is not directed to a natural phenomena and there are genuine issues of material facts whether the ordered combination of the steps of Claim 125, when taken as a whole, is routine and conventional.

The parties do not make separate arguments with respect to Claim 132. For the same reasons as above, the Court holds that Claim 132, which recites "an agent that inhibits cell lysis,"

is not directed to a natural phenomenon and there are genuine issues of material fact whether Claim 132, when taken as a whole, is routine and conventional.

III. CONCLUSION

For the foregoing reasons, the Court **DENIES** Natera's Motion for Summary Judgement of Invalidity under Mayo Step 1(Dkt. 340).

SIGNED this 12th day of January, 2024.

ALAN D ALBRIGHT
UNITED STATES DISTRICT JUDGE